Study Protocol

Validation of a computational model to estimate patient anterior-posterior dimension from an abdominal radiograph

Study Acronym	**VocMepAdar**
Sponsor	**University of Dundee and NHS Tayside**
Sponsor R&D Number	2017RA01
Chief Investigator Principal Investigator	Sarah Vinnicombe Mark Worrall
REC Number	237832
Clinicaltrials.gov ID	NCT03341546
Version Number and Date	1.1, 22nd December 2017

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PROTOCOL APPROVAL

Validation of a model to estimate patient anterior-posterior dimension from an abdominal radiograph

Signatures

By signing this document I am confirming that I have read, understood and approve the protocol for the above study.

Dr Sarah Vinnicombe Chief Investigator	Signature	Date
Mark Worrall Individual Responsible for Statistical Review	Signature	Date

LIST OF ABBREVIATIONS

GCP	Good Clinical Practice
SMF	Study Master File
SOP	Standard Operating Procedure
CNORIS	Clinical Negligence and Other Risks Scheme
AP	Anterior-posterior

INTRODUCTION

1.1 BACKGROUND

Exposure to ionising radiation is understood to be associated with a small increase in the risk of developing cancer later in life. Therefore, all medical exposures need to be justified to ensure that the benefits from the exposure outweigh the risk, and optimised to ensure that the exposure is as low as reasonably practicable consistent with the intended purpose of the exposure.

Patient dose audit is an important part of the optimisation process. It gives information as to the level of dose received on average for an examination on one x-ray machine, allowing a comparison between multiple x-ray machines on the same site and between sites. For all commonly undertaken examinations, national reference levels exist; these are created from local data from all over the UK. Any institution is able to compare their local performance against these national values and determine if they are in line with average national performance of if urgent optimisation is required.

Whereas a patient dose audit for adult x-ray examinations requires only limited information relating to the exposure factors used and the amount of radiation measured by the equipment as delivered to the patient, the method for paediatric patient dose audit also requires a measurement of patient size to be made. This measurement should be either the anterior-posterior or lateral depth of the patient, depending on the examination projection. Alternatively, a measurement of height and weight can be made, from which can be estimated the equivalent cylindrical diameter of the patient, which is equivalent to the measured depth.

National data collection exercises have revealed that these measurements are not being routinely made for paediatric patients undergoing x-ray examinations however. This has meant that no national reference levels have been proposed for paediatric x-rays since 2000. Since 2000, there have been significant technological improvements to the equipment used for x-ray imaging throughout the UK, so these reference values are out of date.

The lack of up to date reference values is affecting efforts to optimise paediatric x-ray exposures across the UK, despite this being the patient cohort for whom optimisation is most important.

1.2 RATIONALE FOR STUDY

A non-commercial computational model has been developed in-house to estimate the patient's anterior-posterior or lateral depth using the radiographic image and the known exposure factors with which it was undertaken. This model has been tested using single composition phantoms and found to be accurate. If it was found to be accurate for real clinical examinations, this would automate the measurement of patient size and give local institutions the additional estimate of patient size required for local patient dose audit. In turn, this would provide the national data required to propose national reference values for paediatric x-ray examinations, which would give all local institutions an important comparator for their performance. This would lead to optimisation in those sites most requiring it; nationally, paediatric x-ray imaging would improve in time.

This pilot study is necessary to determine if the computational model is accurate enough to be relied upon.

2. STUDY OBJECTIVES

2.1 OBJECTIVES

2.1.1 Primary Objective

To determine how accurate the computational model is at determining the patient's anterior-posterior abdomen depth using the radiographic image and the known exposure factors with which it was acquired. Accuracy will be determined by comparing this result with an actual measurement of the patient's anterior-posterior abdomen depth made at the time of the examination.

2.1.2 Secondary Objectives

Any systematic inaccuracy found in the study could be used to further improve the values used in the computational model.

2.2 OUTCOMES

2.2.1 Primary Outcomes

A measure of the accuracy with which the computational model estimates the anterior-posterior depth of patients undergoing abdominal x-ray examinations.

2.2.2 Secondary Outcomes

Any identified systematic inaccuracy could be used to further improve the values used in the computational model.

3. STUDY DESIGN

3.1 STUDY DESCRIPTION

Willing volunteers will be found from patients who have been referred for an AP abdomen x-ray examination in the Radiology department at Ninewells Hospital. Any patient suffering severe abdominal pain when attending for the examination will be excluded as it will be necessary for light physical contact to be made with the patient's abdomen. Any patient that has had an injection of contrast media within the previous 24 hours will be excluded from the study as the computational model is not equipped to work with the presence of contrast media at present.

When the patient reports to main reception, if their attendance is for an AP abdomen x-ray the receptionist will give them the PIS and a reply slip saying that if they wish to take part in the study after having read the PIS they should inform the receptionist. The receptionist will then contact the PI who will be in the radiology department.

When it is time for the volunteer's examination, a radiographer will collect them from the waiting area as normal and bring them to the x-ray room as normal. Their examination will be performed on the Fuji Digital Radiography mobile x-ray machine in room D of main radiology at Ninewells Hospital.

Each patient will be assigned a unique numerical study ID that will be used to correlate the measurement of their anterior-posterior depth with their anonymised image.

The patient will lie on the x-ray couch in room D in the examination position, as directed by the radiographic staff. A measurement of the patient's AP abdomen depth will be made using a device that will attach to the side of the x-ray couch. This device is non-commercial and made in-house. It is not CE marked. Physical contact with the patient will be minimal; a wooden bar will rest gently on their abdomen. This will allow the AP abdomen depth to be read on the scale that is affixed to the x-ray couch.

This measurement will be recorded alongside the clinical indication for the patient under an anonymous and unique participant ID on a patient study form.

The AP abdominal x-ray examination will be undertaken by radiographic staff in accordance with local protocol and with no influence from this study. On completion, the patient's x-ray image will be transferred to PACS as normal, where it will be available for radiologist reporting. The patient will leave the department as normal with no additional request made of them for this study.

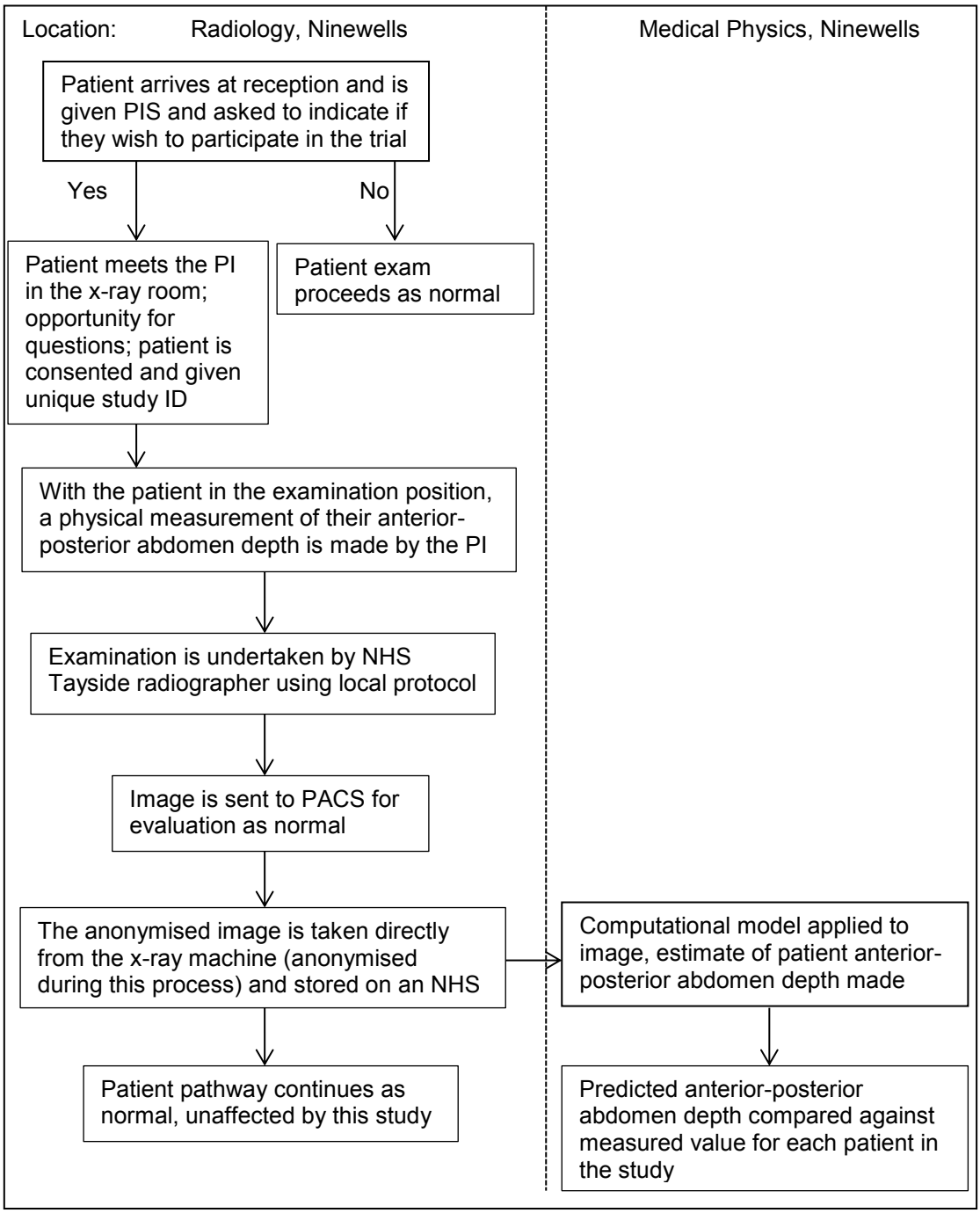
The anonymised patient's x-ray image will be removed directly from the x-ray equipment using an NHS password protected USB memory stick. During this transfer, the software on the x-ray equipment will anonymise the image. This process has been checked using test

patients – the anonymisation process is complete – no patient identifiable information will be left on the image or within the electronic header.

The image will be transferred from the USB memory stick to an NHS Tayside password protected computer. From there, the necessary measurements will be made to allow the computational model to be used to estimate the patient's AP abdomen depth. This estimate will be compared to the physical measurement of AP abdomen depth made for the corresponding patient as recorded on the patient study form – this will determine the accuracy of the estimate.

There is no need for any patient follow up. Individual patients will only participate in the trial once. As this is a pilot study, 20 patients will be recruited in total. This will be enough as an initial cohort to determine whether the computational model is accurate enough to merit further clinical investigation, or if it is in need of adjustment.

3.2 STUDY FLOWCHART



3.3 STUDY MATRIX

Time	At the time of the x-ray exam
Measurement of AP abdomen depth	x

4. STUDY POPULATION

4.1 NUMBER OF PARTICIPANTS

As this is a pilot study, 20 patients will be required after any drop outs. This will be enough as an initial cohort to determine whether the computational model is accurate enough to merit

further clinical investigation, or if it is in need of adjustment. It would be prudent to aim for an even male/female split.
As there is no patient follow-up, the patient's trial recruitment ends when they leave the Radiology department having had their abdomen x-ray examination.
If any participant chooses to withdraw from the study after their x-ray examination, their data will be deleted from the study database. These participants will be replaced to ensure 20 participants overall.

4.2 INCLUSION CRITERIA

Any ambulatory patient attending Ninewells Hospital's Radiology department for an AP abdomen x-ray who does not have contrast media present.
Patients must be over 16 years old.

4.3 EXCLUSION CRITERIA

Patient's presenting with severe abdominal pain at the time of their examination, patients who have had contrast media injected within the last 24 hours and patients who are unable to give their consent.

5. PARTICIPANT SELECTION AND ENROLMENT

5.1 IDENTIFYING PARTICIPANTS

Willing volunteers will be found from patients who have been referred for an AP abdomen x-ray examination in the Radiology department at Ninewells Hospital. When the patient reports to main reception, if their attendance is for an AP abdomen x-ray the receptionist will give them the PIS and a reply slip that should be completed if they wish to take part in the study after having read the PIS given back to the receptionist. The receptionist will then pass a reply slip to the PI who will be in the radiology department.

5.2 CONSENTING PARTICIPANTS

When it is time for the volunteer's examination, a radiographer will collect them from the waiting area as normal and bring them to the x-ray room as normal. Their examination will be performed on the Fuji Digital Radiography mobile x-ray machine in room D of main radiology at Ninewells Hospital. In the privacy of the x-ray room, the PI will answer any questions relating to the study and consent the patient,
Although there isn't much time between the patient receiving the PIS and being consented (a minimum of half an hour), the PIS for this study is not lengthy or complex and the details of what the study entails are not difficult to explain or understand. The patient's only interaction with the PI is at the time of their AP abdomen examination. For all of these reasons, it is felt that the reduced time period between the patient being given the PIS and being consented is appropriate and that it will not impact upon the patient's ability to give informed consent.

In addition, since the patients who attend for AP abdomen x-ray examinations at Ninewells Hospital are referred from all over the Hospital and the wider Dundee area, there is no controlled means of delivering the PIS to the patient at any prior stage.
This is proportionate and commensurate with the research being undertaken

Where a participant requests to speak with a physician from the study team the consent process will not be completed until the participant has spoken to the physician and had all their questions answered to their satisfaction.

The informed consent process will be conducted in compliance with TASC SOP07: Obtaining Informed Consent from Potential Participants in Clinical Research.

5.3 SCREENING FOR ELIGIBILITY

Any patient who is undergoing an AP Abdomen x-ray examination in the main radiology department at Ninewells Hospital is eligible to participate as long as they are not in acute abdominal pain at the time of the examination and have not had an injection of contrast media within the previous 24 hours.

5.4 INELIGIBLE AND NON-RECRUITED PARTICIPANTS

Patients who are in acute abdominal pain, who have had an injection of contrast media within the previous 24 hours or who decline to take part in the study will have their AP Abdomen x-ray examination as normal with no involvement from the principal investigator.

5.4.1 Withdrawal procedures

Study recruitment only lasts as long as it takes to perform an AP Abdomen x-ray examination; withdrawal will not be necessary for any patient.
If a patient were to change their mind about participation after their examination, their study data will be removed from the anonymised research database.

6. STUDY & SAFETY ASSESSMENTS

There are no specific safety assessments necessary for participation in this study; the measurement of AP abdomen depth does not pose any risk and the patient will simply undergo an AP Abdomen x-ray examination as per their referral.

7. DATA COLLECTION & MANAGEMENT

7.1 DATA COLLECTION

The patient's sex and clinical indication (i.e. the reason given for the AP abdomen x-ray examination on the request) will be recorded along with the physical measurement of their AP abdomen depth.
These 3 variables will be recorded at the time of the x-ray examination by the principal investigator on the patient study form. The patient's x-ray image will be taken directly from the x-ray equipment by the principal investigator; the image is anonymised during this transfer process.

7.2 DATA MANAGEMENT SYSTEM

As there is no complex analyses necessary, the anonymised data will be stored on a Microsoft Excel spreadsheet on an NHS Tayside computer.

Data management will be conducted in compliance with TASC SOPs on Data Management, including TASC SOP53 Data Management Systems in Clinical Research and TASC SOP48 Data Management in CTIMPs using Excel.
The data management system (DMS) will be Excel as approved by Sponsor. The DMS will be based on the protocol and Participant Study Form for the study and individual requirements of the investigators. The Participants Study Form will collect only information that is required to meet the aims of the study and to ensure the eligibility and safety of the participant. The study database will be compliant with TASC SOP53.

The database is managed in line with all applicable principles of medical confidentiality and UK law on data protection, namely, the Data Protection Act 1998, which brought UK law into line with the EU Data Protection Directive. The Data Controller will be the NHS Tayside and the Data Custodian will be the PI.

The CI may delegate Participant Study Form completion but is responsible for completeness, plausibility and consistency of the Participant Study Form. Any queries will be resolved by the CI or delegated member of the study team.

Database lock will be conducted in compliance with TASC SOP32 Locking Clinical Study Databases

8. STATISTICS AND DATA ANALYSIS

8.1 SAMPLE SIZE CALCULATION

The sample size for this pilot study will be 20 patients. There is no statistical aim or calculation in deriving this number; 20 is simply a high enough number as to allow for confidence in the computational model where all or most results are found to be individually accurate.

8.2 PROPOSED ANALYSES

Analyses is straightforward; the difference between the computationally predicted AP abdomen depth and that measured for each individual participant will be expressed as a percentage. Some statistical analyses will be undertaken on the 20 individual results (average, median, minimum and maximum deviations). A t-test will be used to compare predicted and measured results.
All analyses will be undertaken by the principal investigator using Microsoft Excel and IBM SPSS.

8.3 MISSING DATA

It is not reasonably foreseeable that there will be any missing data. What little data there is to be recorded will not leave Ninewells Hospital and will be input into an electronic record very soon after it is acquired.

8.4 TRANSFER OF DATA

Data will not leave Ninewells Hospital, either physically or electronically.

9. STUDY MANAGEMENT AND OVERSIGHT ARRANGEMENTS

9.1 STUDY MANAGEMENT GROUP

The study will be co-ordinated by a Study Management Group, consisting of the chief investigator and the principal investigator.

9.2 STUDY MANAGEMENT

The principal investigator will oversee the study and will be accountable to the CI. The PI will be responsible for checking the study data forms for completeness, plausibility and consistency. However, this remains the overall responsibility of the CI. Any queries will be resolved by the CI or delegated member of the study team.

A study-specific Delegation Log will be prepared for each site, detailing the responsibilities of each member of staff working on the study.

9.3 STUDY STEERING COMMITTEE

A Trial Steering Committee (TSC) will be established to oversee the conduct and progress of the study. The terms of reference of the TSC, the draft template for reporting are detailed in Appendix 1.

9.4 DATA MONITORING COMMITTEE

An independent Data Monitoring Committee (DMC) will be established to oversee study progress. The terms of reference of the DMC are detailed in Appendix 2.

9.5 INSPECTION OF RECORDS

The CI, PIs and all institutions involved in the study will permit study related monitoring, audits, and REC review. The CI agrees to allow the Sponsor or, representatives of the Sponsor, direct access to all study records and source documentation.

10. GOOD CLINICAL PRACTICE

10.1 ETHICAL CONDUCT OF THE STUDY

The study will be conducted in accordance with the principles of good clinical practice (GCP).

In addition to Sponsorship approval, a favorable ethical opinion will be obtained from the appropriate REC and appropriate NHST R&D approval will be obtained prior to commencement of the study.

10.1.1 Confidentiality

All laboratory specimens, evaluation forms, reports, and other records will be identified in a manner designed to maintain participant confidentiality. All records will be kept in a secure storage area with limited access to study staff only. Clinical information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the Sponsor or its designee. The CI and study staff involved with this study will not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee will be obtained for the disclosure of any said confidential information to other parties.

10.1.2 Data Protection

The CI and study staff involved with this study will comply with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles. The CI and study staff will also adhere, if appropriate, to the current version of the NHS Scotland Code of Practice on Protecting Patient Confidentiality. Access to collated participant data will be restricted to the CI and appropriate study staff.

Computers used to collate the data will have limited access measures via user names and passwords.

Published results will not contain any personal data that could allow identification of individual participants.

10.1.3 Insurance and Indemnity

The University of Dundee and Tayside Health Board are Co-Sponsoring the study.

Insurance – The University of Dundee will obtain and hold a policy of Public Liability Insurance for legal liabilities arising from the study.

Tayside Health Board will maintain its membership of the Clinical Negligence and Other Risks Insurance Scheme ("CNORIS") which covers the legal liability of Tayside in relation to the study.

Where the study involves University of Dundee staff undertaking clinical research on NHS patients, such staff will hold honorary contracts with Tayside Health Board which means they will have cover under Tayside's membership of the CNORIS scheme.

Indemnity The Co-Sponsors do not provide study participants with indemnity in relation to participation in the Study but have insurance for legal liability as described above.

11. STUDY CONDUCT RESPONSIBILITIES

11.1 PROTOCOL AMENDMENTS, DEVIATIONS AND BREACHES

The CI will seek approval for any amendments to the Protocol or other study documents from the Sponsor, REC and NHS Tayside R&D Office. Amendments to the protocol or other study docs will not be implemented without these approvals.

In the event that a CI needs to deviate from the protocol, the nature of and reasons for the deviation will be recorded in the SMF, documented and submitted to the Sponsor. If this necessitates a subsequent protocol amendment, this will be submitted to the Sponsor for approval and then to the appropriate REC and lead NHS R&D Office for review and approval.

In the event that a serious breach of GCP is suspected, this will be reported to the Sponsor immediately using the form "Notification to Sponsor of Serious Breach or Serious Deviation".

11.2 STUDY RECORD RETENTION

Archiving of study documents will be for five years after the end of study.

11.3 END OF STUDY

The end of study is defined as last patient last visit (LPLV). The Sponsor, CI and/or the TSC have the right at any time to terminate the study for clinical or administrative reasons.

The end of the study will be reported to the Sponsor and REC within 90 days, or 15 days if the study is terminated prematurely. The CI will ensure that any appropriate follow up is arranged for all participants.

A summary report of the study will be provided to the Sponsor and REC within 1 year of the end of the study.

12. REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

12.1 AUTHORSHIP POLICY

Ownership of the data arising from this study resides with the study team and their respective employers. On completion of the study, the study data will be analysed and tabulated, and a clinical study report will be prepared.

12.2 PUBLICATION

The clinical study report will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing the results of the study.

Summaries of results will also be made available to Investigators for dissemination within their clinical areas (where appropriate and according to their discretion).

12.3 PEER REVIEW

The protocol will be subject to critical review by the academic and clinical supervisors on behalf of the University of Dundee as majority funder of the research.

The PhD was reviewed and accepted by a University of Dundee PhD committee before the principal investigator commenced work.

13. REFERENCES

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3. Hart D, Hillier M C, Wall B F. *W14 – Doses to patients from medical x-ray examinations in the UK – 2000 review*. NRPB 2002.
4. Hart D, Hillier M C, Wall B F. *29 – Doses to patients from radiographic and fluoroscopic x-ray imaging procedures in the UK – 2005 review.* HPA 2007.
5. Hart D, Hillier M C, Shrimpton P C. *34 – Doses to patients from radiographic and fluoroscopic x-ray imaging procedures in the UK – 2010 review.* HPA 2012